09872705

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SESSION RESUMED IN FILE 'HCAPLUS' AT 17:29:40 ON 26 APR 2005
FILE 'HCAPLUS' ENTERED AT 17:29:40 ON 26 APR 2005
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-38.69	-38.69

```
=> s testosterone ether
         57193 TESTOSTERONE
        459975 ETHER
L5           5 TESTOSTERONE ETHER
                 (TESTOSTERONE(W)ETHER)
```

=> d l5 1-5 ibib hitstr abs

L5 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:423438 HCAPLUS
DOCUMENT NUMBER: 127:90716
TITLE: Effects of repeated ether stress on the hypothalamic-pituitary-testes axis in adult rats with special reference to inhibin secretion
AUTHOR(S): Tohei, Atsushi; Tomabechi, Taeko; Mamada, Masayuki; Akai, Makoto; Watanabe, Gen; Taya, Kazuyoshi
CORPORATE SOURCE: Laboratory of Veterinary Physiology, Tokyo University of Agriculture and Technology, Fuchu, 183, Japan
SOURCE: Journal of Veterinary Medical Science (1997), 59(5), 329-334
CODEN: JVMSEQ; ISSN: 0916-7250
PUBLISHER: Japanese Society of Veterinary Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Effects of ether stress on the hypothalamo-hypophysial-gonadal axis in adult male rats were examined To clarify the role of adrenal glucocorticoids in gonadal function, the effects of adrenalectomy and Dexamethasone treatment were also investigated. Ether stress increased the plasma concns. of ACTH and corticosterone, but decreased the plasma concns. of LH, FSH, inhibin and testosterone. The pituitary responsiveness to LH-RH for LH release and testicular responsiveness to the endogenous LH for testosterone release were maintained in stressed rats. Adrenalectomy caused an increase in the plasma concns. of ACTH, but decreased the plasma concns. of LH, FSH and testosterone. Dexamethasone

treatment in adrenalectomized rats recovered the levels of plasma gonadotropins to control levels. The concentration of plasma inhibin did not change in adrenalectomized rats, but it was decreased compared to control rats by Dexamethasone treatment. Treatments of Dexamethasone in intact male rats resulted in a decline in plasma levels of testosterone and inhibin without a decrease in the levels of LH and FSH, indicating the direct effect of Dexamethasone on the testes. These results indicate that increased ACTH secretion in stressed rats is probably due to hypersecretion of CRH from the hypothalamus, which suppresses gonadotropin secretion via the inhibition of LH-RH. The decreased levels of testosterone may be caused by a stress-induced decrease in plasma LH concns. and increased secretion of corticosterone in the ether stressed rats. The low levels of plasma inhibin in stressed rats was also probably due to the direct effect of corticosterone on the Sertoli cells.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:506 HCAPLUS
DOCUMENT NUMBER: 84:506
TITLE: Evaluation of the resorptive skin action of testosterone and its ethers
AUTHOR(S): Fedorov, V. K.; Shashkina, L. F.
CORPORATE SOURCE: Lab. Prom. Toksikol., Vses. Nauchno-Issled. Khim.-Farm. Inst. im. Ordzhonikidze, Kupavna, USSR
SOURCE: Farmakologiya i Toksikologiya (Moscow) (1975), 38(5), 596-9
CODEN: FATOAO; ISSN: 0014-8318
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB Testosterone propionate [57-85-2] > testosterone enanthate [315-37-7] > testosterone (I) [58-22-0] > testosterone phenylpropionate [1255-49-8] > testosterone isocaproate [15262-86-9] > testosterone caprinate [5721-91-5] were absorbed by the skin of rats. The maximum effect (increase in seminal vesical and prostate wts.) was observed 2-3 days after a single topical application. The min. effective dose was 0.1 mg/animal.

L5 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1975:558153 HCAPLUS
DOCUMENT NUMBER: 83:158153
TITLE: Synthesis and biological activity of some ethers of testosterone. Implications concerning the biological activity of esters of testosterone
AUTHOR(S): Solo, Alan J.; Bejba, Natalie; Hebborn, Peter; May, Marian
CORPORATE SOURCE: Sch. Pharm., State Univ. New York, Buffalo, NY, USA
SOURCE: Journal of Medicinal Chemistry (1975), 18(2), 165-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The allyl (I) [20860-14-4], benzyl [20860-15-5], 2,3-dihydroxypropyl (II) [54914-67-9], 3-hydroxypropyl [50301-52-5], 4-pentenyl [54914-65-7], pentyl [54914-66-8], and propyl [50393-37-8] ethers of testosterone were prepared by O-alkylation of 3,3-ethylenedioxyandrost-5-en-17β-ol [975-57-5] followed by hydrolysis. The ethers had much less anabolic or androgenic activity than testosterone Me ether [13990-32-4], however all

but II are effective inhibitors of testosterone 5α-reductase [9036-43-5]. Structure-activity relations are discussed.

L5 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1969:104967 HCAPLUS
DOCUMENT NUMBER: 70:104967
TITLE: Reduction of testicular testosterone in rats by ether anesthesia
AUTHOR(S): Fariss, Bruce; Hurley, Timothy J.; Hane, Satoshi; Forsham, Peter H.
CORPORATE SOURCE: Med. Center, Univ. of California, San Francisco, CA, USA
SOURCE: Endocrinology (1969), 84(4), 940-2
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There was a reduction of testicular testosterone in rats given ether anesthesia, occurring within 2 min. and maintained for at least 24 hrs. The testosterone content of the testicles was essentially the same for animals sacrificed at 2, 5, 10, and 15 min., and 4 and 24 hrs. after ether anesthesia.

L5 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1951:50693 HCAPLUS
DOCUMENT NUMBER: 45:50693
ORIGINAL REFERENCE NO.: 45:8651f-i
TITLE: Relation between chemical constitution and biological activity. New vasodilators and synthetic curare compounds derived from sex hormones
AUTHOR(S): Cavallini, G.; Massaran, E.
CORPORATE SOURCE: Maggioni & Co., Milan, Italy
SOURCE: Farm. sci. e tec. (Pavia) (1951), 6, 291-9
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Et2NC2H4 ethers of sterols were prepared by heating suspensions in 30% KOH with an excess of Et2NC2H4Cl at 100°, extraction of the oil with Et2O, evaporation and precipitation with HCl in EtOH. The HCl salt of the α-estrone ether (I) m. 190-1°, the 2 HCl salt of the di-ether of estradio (II) m. 183-4°, is soluble in H2O, EtOH, MeOH, CHCl3, and Me2CO, insol. in C6H6; the HCl salt of the **testosterone ether** (III), m. 165-6°, is soluble in the same solvents; the HCl salt of the ether of trans-Δ5-6-dehydroandrosterone (IV), m. 200-1°, is soluble in the same solvents; the 2HCl salt of the double ether of Δ5-6-trans-trans-androstenediol (V), m. 255-6°, is soluble in H2O, EtOH, MeOH, CHCl3 and insol. in Me2CO and C6H6. Heating the base of the ethers with MeI in EtOH and evaporation gives the corresponding MeI compds. of which that of I m. 231-2° and has the same solubility as V; of II m. 225-6°, is soluble in H2O, EtOH, MeOH, insol. in CHCl3, Me2CO and C6H6; of III m. 200-1°, is soluble in H2O, EtOH, MeOH, Me2CO and CHCl3, insol. in C6H6; of IV m. 166-7°, has the same solys.; of V m. 246-8°, is soluble in H2O, EtOH, MeOH, CHCl3, insol. in Me2CO and C6H6. I, II, III, IV and V are strong coronary vasodilators, the MeI compds. of II and V have strong curare-like action.

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(FILE 'HOME' ENTERED AT 16:42:20 ON 26 APR 2005)

FILE 'STNGUIDE' ENTERED AT 16:42:25 ON 26 APR 2005

FILE 'HCAPLUS' ENTERED AT 16:42:37 ON 26 APR 2005
L1 57193 S TESTOSTERONE
L2 48 S L1 AND PRODRUG
L3 6 S L2 AND ETHER
L4 17 S L2 AND ESTER
L5 5 S TESTOSTERONE ETHER
L6 185 S TESTOSTERONE ESTER
L7 4 S L6 AND COMPOSITION

=> s l6 and androgen
29281 ANDROGEN
L8 32 L6 AND ANDROGEN

=> d l8 1-5 ibib hitstr abs

L8 ANSWER 1 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:908416 HCAPLUS
DOCUMENT NUMBER: 140:139706
TITLE: Estimating the contribution of the prostate to blood dihydrotestosterone
AUTHOR(S): Toorians, Arno W. F. T.; Kelleher, Sharyn; Gooren, Louis J.; Jimenez, Mark; Handelsman, David J.
CORPORATE SOURCE: Department of Endocrinology / Andrology, Vrije Universiteit University Medical Center, Amsterdam, 1007 MB, Neth.
SOURCE: Journal of Clinical Endocrinology and Metabolism (2003), 88(11), 5207-5211
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The prostate strongly expresses type 2 5α-reductase, which avidly converts on entry most testosterone (T) to 5α-dihydrotestosterone (DHT). However, the quant. contribution of the prostate to blood DHT is uncertain. The authors evaluated prostatic contribution to blood DHT by comparing the blood DHT concns. in **androgen**-deficient patients with or without a prostate while they were receiving standard dose of T replacement. **Androgen**-deficient males (ADM) and female to male (F2M) transsexuals were studied in 2 centers, with both groups receiving either **testosterone ester** injections (250 mg mixed T esters) every 1 wk (Amsterdam) or 800 mg subdermal T implantation (Sydney). Among 39 Dutch patients, F2M (n = 21) were younger and smaller in physique than ADM (n = 18). One week (±1 d) after an injection, plasma DHT concns. were 1.6±0.2 (F2M) vs. 1.4±0.2 (ADM) nmol/L (P = 0.47), but the postinjection time interval to blood sampling was shorter in F2M (5.9±0.4 vs. 7.2±0.3 d; P = 0.01). Covariance adjustment for time since last injection, age, and physique did not change the lack of significant difference in postinjection plasma DHT concentration The rapid and wide excursions in plasma T concns. after an i.m. T ester injection make the timing of blood sampling critical To remove confounding by this variable, the experiment was repeated at a second site in similar patients, but using a depot T that achieves steady-state delivery for prolonged periods. Among 29 Australian patients, before and 1 mo after subdermal implantation

of 800 mg T, plasma DHT concns. were not significantly different between groups [F2M, 1.1±0.1 (n = 14); ADM, 1.3±0.1 (n = 15); P = 0.28]. Correction for covariates, including age, height, weight, body surface area, and body mass index, did not influence the lack of significant difference between treated groups. As both modes of T administration yielded similar plasma DHT concns. regardless of the presence of a prostate, this study indicates that the normal human prostate is not a major contributor to circulating blood DHT concns.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:572154 HCAPLUS
DOCUMENT NUMBER: 139:317648
TITLE: Randomized placebo-controlled trial of **androgen** effects on muscle and bone in men requiring long-term systemic glucocorticoid treatment
AUTHOR(S): Crawford, Bronwyn A. L.; Liu, Peter Y.; Kean, Mary T.; Bleasel, Jane F.; Handelsman, David J.
CORPORATE SOURCE: Department of Endocrinology, ANZAC Research Institute, Sydney, Australia
SOURCE: Journal of Clinical Endocrinology and Metabolism (2003), 88(7), 3167-3176
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Long-term glucocorticoid therapy in men is associated with loss of bone and muscle mass as well as a decrease in serum testosterone. The authors tested the effect of two androgens, testosterone and its minimally aromatizable analog nandrolone, on muscle mass (dual x-ray absorptiometry), muscle strength (knee flexion and extension by isokinetic dynamometry), bone mineral d. (BMD), and quality of life (Qualeffo-41 questionnaire) in 51 men on a mean daily prednisone dose of 12.6±2.2 mg. Men were randomized, double blind, to testosterone (200 mg mixed esters), nandrolone decanoate (200 mg), or placebo given every fortnight by i.m. injection for 12 mo. At 12 mo, both androgens increased muscle mass (mean change from baseline +3.5%, +5.8%, and -0.9% in testosterone, nandrolone, and placebo groups, resp., P < 0.0001) and muscle strength (P < 0.05). Lumbar spine BMD increased significantly only in men treated with testosterone (4.7±1.1%, P < 0.01). There was no significant change in hip or total body BMD. Testosterone, but not nandrolone or placebo, improved overall quality of life (P < 0.001). These results suggest that **androgen** therapy may have a role in ameliorating adverse effects of glucocorticoid therapy such as muscle and bone loss and aromatization is necessary for **androgen** action on bone but not on muscle.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:575757 HCAPLUS
DOCUMENT NUMBER: 137:120058
TITLE: Male contraceptive formulation comprising norethisterone
INVENTOR(S): Nieschlag, Eberhard; Kamischke, Axel; Oettel, Michael; Ruebig, Alexander; Schillinger, Ekkerhard; Ursula-Friederike, Habenicht

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: U.S. Pat. Appl. Publ., 11 pp., Cont.-in-part of U.S. Ser. No. 266,326, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103176	A1	20020801	US 2001-764149	20010119
PRIORITY APPLN. INFO.:			US 2000-266326	B2 20000215

OTHER SOURCE(S): MARPAT 137:120058

AB A formulation for male contraception comprising a progestin possessing both estrogenic and androgenic properties is remarkably effective for spermatogenesis suppression in males. The progestin Norethisterone (NET), particularly its derivs. Norethisterone acetate and Norethisterone enanthate in sufficient doses induce oligozoospermia or azoospermia in males. Formulations further comprising an **androgen**, such as a testosterone derivative such as a **testosterone ester**, particularly testosterone undecanoate, are especially effective male contraceptive formulations.

L8 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:825294 HCAPLUS
DOCUMENT NUMBER: 136:161485
TITLE: Nongenomic steroid action: Inhibiting effects on cell-to-cell communication between rat ventricular myocytes
AUTHOR(S): Verrecchia, Franck; Sarrouilhe, Denis; Herve, Jean-Claude
CORPORATE SOURCE: Physiologie Cellulaire, UMR CNRS 6558, Poitiers, Fr.
SOURCE: Experimental & Clinical Cardiology (2001), 6(3), 124-131
CODEN: ECCAF7; ISSN: 1205-6626
PUBLISHER: Pulsus Group Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Numerous steroids are now believed to possess rapid membrane effects independent of the classical gene activation pathways and are potent modulators of membrane proteins, including voltage-and ligand-operated channels. The effects of steroids on the functional state of the intercellular channels clustered in gap junctions were compared by estimation of either the permeability for a fluorescent dye or the elec. conductance in cardiac myocytes of newborn rat. At 25 μM, the esters of 17β-estradiol, testosterone and two other **androgen** hormones rapidly abolished cell-to-cell communication, whereas none of the longer chain steroids, belonging to pregnane (17α-hydroxypregnenolone, hydrocortisone), sterol (cholesterol, 25-hydroxycholesterol), bile acid (cholic and lithocholic acids) and vitamin (D3) families, lowered the junctional permeability. Altogether, no correlation with the presence or position of double bonds nor with the trans- or cis-fusion of the A and B rings was recognized. Esterification was a prerequisite for the activity of extracellularly applied steroids but the number, nature and position of ester chain(s) had no influence. 17β-Estradiol or testosterone effects were not prevented when cells were preincubated with blockers of the estrogen or **androgen** nuclear receptors (tamoxifen and

cyproterone acetate, resp.). This, together with the rapid time course of the steroid effect (complete within a few minutes), in a rather high active concentration range, suggests a nongenomic mechanism of action. The reversible uncoupling effect of steroids appears to be independent of the shape of the mols. and more probably related to their size and liposoly., which condition their insertion into the lipid bilayer and their subsequent disturbing effects.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:617831 HCAPLUS
DOCUMENT NUMBER: 135:176045
TITLE: Male contraceptive formulations comprising norethisterone or NET derivatives alone or in combination with an **androgen**
INVENTOR(S): Nieschlag, Eberhard; Kamischke, Axel; Oettel, Michael; Ruebig, Alexander; Schillinger, Ekkerhard; Habenicht, Ursula-Friederike
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060376	A1	20010823	WO 2001-IB188	20010215
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2398063	AA	20010823	CA 2001-2398063	20010215
EP 1267885	A1	20030102	EP 2001-902590	20010215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001008411	A	20030311	BR 2001-8411	20010215
JP 2003522795	T2	20030729	JP 2001-559472	20010215
EE 200200454	A	20031215	EE 2002-454	20010215
NO 2002003607	A	20021015	NO 2002-3607	20020730
BG 107066	A	20030530	BG 2002-107066	20020905

PRIORITY APPLN. INFO.: EP 2000-200493 A 20000215
US 2000-503729 A 20000215
WO 2001-IB188 W 20010215

AB A formulation for male contraception comprising a progestin possessing both estrogenic and androgenic properties is remarkably effective for spermatogenesis suppression in males. The progestin Norethisterone (NET), particularly its derivs. Norethisterone acetate and Norethisterone enanthate in sufficient doses induce oligozoospermia or azoospermia in males. Formulations further comprising an **androgen**, such as a

testosterone derivative such as a **testosterone ester**, particularly testosterone undecanoate, are especially effective male contraceptive formulations.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l8 6-15 ibib hitstr abs

L8 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:416217 HCAPLUS
DOCUMENT NUMBER: 135:252094
TITLE: Effects of **androgen** deficiency and replacement on prostate zonal volumes
AUTHOR(S): Jin, B.; Conway, A. J.; Handelsman, D. J.
CORPORATE SOURCE: Department of Andrology, University of Sydney, Sydney, 2006, Australia
SOURCE: Clinical Endocrinology (Oxford, United Kingdom) (2001), 54(4), 437-445
CODEN: CLECAP; ISSN: 0300-0664
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Androgens play a key role in prostate development and disease. However the effects of **androgen** deficiency and replacement on the prostate during mid-life are not well understood, and there is no information on their effects on prostate zonal vols. This study aimed to define the effects of **androgen** deficiency and **androgen** replacement therapy on prostate zonal vols. (central, peripheral & total) using planimetric prostate ultrasound with particular emphasis on the central zone of the prostate, the most hormonally sensitive and fastest growing region of the prostate and the zone where nodular benign prostate hyperplasia originates. Central and total prostate volume were measured directly, and peripheral prostate volume calculated, by a single observer using transrectal ultrasound in 71 hypogonadal men (aged 40 ± 2, range 18-78 yr) who were compared with individually age-matched health controls without prostate or gonadal disease. Among the men with **androgen** deficiency, 17 men had untreated **androgen** deficiency (never treated or no treatment for at least 6 mo) and 54 men were receiving long-term **androgen** replacement therapy (median 32 mo, 93% ≥ 6 mo) with testosterone implants (n = 27), **testosterone ester** injections (n = 24) or other testosterone treatment (n = 3). RESULTS Compared with individually age-matched controls, untreated **androgen** deficient men (n = 17) had reduced central (4.0 ± 0.5 vs. 6.2 ± 0.5 mL, P < 0.001) and total (23.4 ± 2.6 vs. 29.2 ± 1.6 mL, P < 0.001) prostate vols. whereas the reduction in peripheral prostate volume (19.4 ± 2.1 vs. 23.0 ± 1.3 mL, P = 0.15) was not statistically significant. Men with treated **androgen** deficiency (n = 54) also still had significantly reduced central (4.8 ± 0.4 vs. 6.8 ± 0.4, P < 0.001), peripheral prostate volume (19.6 ± 0.8 vs. 21.6 ± 0.7 mL, P = 0.06) and total (24.4 ± 1.1 vs. 28.4 ± 1.0 mL, P = 0.008) despite prolonged restoration of physiol. testosterone concns. Neither modality of testosterone treatment nor type of hypogonadism influenced prostate zonal vols. before or after treatment. In contrast, central, peripheral and total prostate volume increased with age among healthy controls and men with **androgen** deficiency regardless of **androgen** replacement therapy. Plasma PSA concns. were reduced in men with untreated **androgen** deficiency and were similar to age-matched

controls in men with treated **androgen** deficiency. We conclude that, during mid-life, chronic **androgen** deficiency due to hypogonadism is associated with reduced central, peripheral and total prostate vols. Reduced prostate vols. persist even during long-term maintenance of effective **androgen** replacement therapy with physiol. testosterone concns. until the fourth decade of life. After that, prostate vols. increase with age regardless of **androgen** deficiency or replacement. These findings suggest that, during mid-life, age is a more important determinant of prostate growth than ambient testosterone concns. maintained in the physiol. range. The persistently subnormal prostate vols. despite adequate **androgen** replacement therapy may explain the apparent paucity of cases of overt prostate disease among testosterone-treated **androgen** deficient men who retain protection against prostate disease despite physiol. **androgen** replacement therapy.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:80595 HCAPLUS
DOCUMENT NUMBER: 134:126210
TITLE: Testosterone-induced inhibition of spermatogenesis is more closely related to suppression of FSH than to testicular **androgen** levels in the cynomolgus monkey model (Macaca fascicularis)
AUTHOR(S): Weinbauer, G. F.; Schlatt, S.; Walter, V.; Nieschlag, E.
CORPORATE SOURCE: Institute of Reproductive Medicine, University of Munster, Munster, D-48129, Germany
SOURCE: Journal of Endocrinology (2001), 168(1), 25-38
CODEN: JOENAK; ISSN: 0022-0795
PUBLISHER: Society for Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have investigated the antigonadotropic and antispermatogenic effects of exposure to a long-acting **testosterone ester** in the cynomolgus monkey model. Groups of five adult animals were exposed either to vehicle or to 10 mg/kg or 20 mg/kg testosterone buciclate (TB) over a 26-wk period with injections given in weeks 0, 11 and 18. In week 26, testicular biopsy tissue was collected. Serum testosterone levels were in the upper normal range with 10 mg/kg TB and were approx. twofold higher with 20 mg/kg TB. The estradiol pattern followed that of testosterone and body wts. increased in a testosterone-dependent manner. TB completely abolished serum LH bioactivity. Serum concns. of FSH and inhibin-α were suppressed in a TB dose-dependent manner. During weeks 4-8 after the first injection, a rebound of FSH and inhibin but not bioactive LH secretion occurred. This rebound was followed immediately by a restimulation of testis size and sperm nos. After the next TB injections these parameters were once again suppressed. Nadir testis size was 30-40% of baseline and animals were severely oligozoospermic or transiently azoospermic. Consistent azoospermia was not achieved. Quantitation of serum inhibin B, proliferating cell-nuclear antigen staining and flow cytometric anal. of germ cell populations revealed pronounced suppression of spermatogenesis in both TB-treated groups, whereas **androgen** receptor expression remained unchanged. Testicular androgens levels, determined in week 26, did not differ among all three groups and did not correlate with sperm nos., histol. and immunocytochem. findings. All suppressive effects were fully reversed

during the recovery period. The authors have concluded that pronounced suppression of primate spermatogenesis seemingly requires inhibition of FSH rather than testicular **androgen** levels, at least in this preclin. non-human primate model. For the purpose of male contraception, FSH inhibition appears mandatory.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:883675 HCAPLUS
DOCUMENT NUMBER: 135:71330
TITLE: Steroidal contraception for men
AUTHOR(S): Sarkar, N. N.
CORPORATE SOURCE: Department of Reproductive Biology, All India Institute of Medical Sciences, New Delhi, 110 029, India
SOURCE: International Journal of Clinical Practice (2000), 54(9), 594-603
CODEN: IJCPF9; ISSN: 1368-5031
PUBLISHER: Medicom International
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 64 refs. This article is a review of the development of male steroidal contraceptives during the past 25 yr. Numerous studies have been conducted on male volunteers with oral and/or injectable prepns. of single or combined steroids. Progestogen, **androgen** alone, or progestogen and **androgen** combinations have been used as weekly or monthly injectable formulations. Most of the studies involved small nos. of subjects. There was reversible suppression of spermatogenesis to oligospermia and/or azoospermia during the treatment period. Alteration of LH, FSH and testosterone levels in the blood was observed in most of these studies, depending on the steroid or combination of steroids used. There were reports about decreased or increased libido and weight gain during treatment with steroids. No other serious side-effects were found. Attention has recently focused on developing an **androgen**-only male contraceptive, because **testosterone ester** has shown promising results. The development of an effective and reliable steroidal contraceptive for men may be possible but this requires further research.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:819250 HCAPLUS
DOCUMENT NUMBER: 132:45441
TITLE: Male contraceptive comprising a prolactin inhibitor and a sex steroid
INVENTOR(S): Lincoln, Gerald Anthony; Wu, Frederick
PATENT ASSIGNEE(S): Medical Research Council, UK
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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WO 9966935 A1 19991229 WO 1999-GB1948 19990621
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9943825 A1 20000110 AU 1999-43825 19990621
PRIORITY APPLN. INFO.: GB 1998-13278 A 19980620
WO 1999-GB1948 W 19990621

AB There is provided a male contraceptive which comprises as active ingredients a prolactin inhibitor and a sex steroid or **androgen.** Quinagolide is a suitable prolactin inhibitor and is conveniently administered daily in oral form. The sex steroid or **androgen** may be testosterone or a **testosterone ester**, which may be administered by injection, as a sub-cutaneous implant or orally. A method of inducing azoospermia in healthy males is also described. Description of administration of testosterone and quinalgolide is given.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:123284 HCAPLUS
DOCUMENT NUMBER: 124:165597
TITLE: Reversible interruption of gap junctional communication by testosterone propionate in cultured Sertoli cells and cardiac myocytes
AUTHOR(S): Pluciennik, F.; Verrecchia, F.; Bastide, B.; Herve, J. C.; Joffre, M.; Deleze, J.
CORPORATE SOURCE: Lab. Physiol. Cell. Physiol. Animale, Poitiers, 86022, Fr.
SOURCE: Journal of Membrane Biology (1996), 149(3), 169-77
CODEN: JMBBBO; ISSN: 0022-2631
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A direct cell-to-cell exchange of ions and mols. occurs through specialized membrane channels built by the interaction of two half channels, termed connexons, contributed by each of the two adjacent cells. The elec. and diffusional couplings have been investigated by monitoring resp. the cell-to-cell conductance and the fluorescence recovery after photobleaching, in Sertoli and cardiac cells of young rats. In both cell types, a rapid impairment of the intercellular coupling has been observed in the presence of testosterone propionate. This interruption of the cell-to-cell communication through gap junction channels was dose-dependent, observed in the concentration range 1 to 25 μM and was progressively reversed after withdrawing the **testosterone ester.** Pretreatment with cyproterone acetate, an antiandrogen which blocks the nuclear testosterone receptor by binding, did not prevent the uncoupling action of the **androgen** ester. This observation, together with the rapid time course of the uncoupling and recoupling, and the rather high effective concentration (micromolar) of the steroid compound, suggests a nongenomic mechanism of action. The uncoupling concns. were very similar to those of other steroid compds. known to interrupt gap junctional communication. The uncoupling could result from a direct

interaction of the steroid with the proteolipidic structure of the membrane, that might alter the conformation of the gap junction channels and their functional state.

L8 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:108014 HCAPLUS
DOCUMENT NUMBER: 124:165503
TITLE: Suppression of testicular and epididymal functions in a non-human primate (bonnet monkey) by combined administration of a gonadotropin-releasing hormone antagonist and testosterone buciclate
AUTHOR(S): Rajalakshmi, M.; Kumar, P. K. Suresh; Kinger, S.; Pal, P. C.; Pruthi, J. S.; Bajaj, J. S.
CORPORATE SOURCE: India
SOURCE: Contraception (1995), 52(6), 381-8
CODEN: CCPTAY; ISSN: 0010-7824
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of a long-acting **androgen**, testosterone buciclate (TB), to induce suppression of testicular and epididymal sperm functions when given in combination with a potent GnRH antagonist (Antide) either on day 1 or 45 of Antide administration (days 1-90) as well as the ability of TB to maintain Antide-induced suppression of spermatogenesis were evaluated in adult bonnet monkeys. A group of untreated animals (group I) acted as controls. All animals given Antide and **androgen** simultaneously (group II) became azoospermic but at different times. When **androgen** administration was delayed 45 days after start of Antide treatment (group III), the mean sperm concentration remained in the normospermic range and only three animals became azoospermic. Antide given alone (group IV) induced azoospermia in three animals and oligospermia in the remaining animals; spermatogenesis recovered when Antide was withdrawn and TB was injected. In all Antide-treated animals (groups II-IV), non-motile spermatozoa or sperm with non-progressive motility and poor gel penetrability were seen in the ejaculate.

L8 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:17688 HCAPLUS
DOCUMENT NUMBER: 124:135769
TITLE: Treatment of hypogonadal men
AUTHOR(S): Anawalt, Bradley D.; Bebb, Richard A.; Matsumoto, Alvin M.
CORPORATE SOURCE: School Medicine, University Washington, Seattle, WA, USA
SOURCE: Current Opinion in Endocrinology & Diabetes (1995), 2(6), 476-82
CODEN: CENDES; ISSN: 1068-3097
PUBLISHER: Current Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 33 refs. The choice of **androgen** therapy for the hypogonadal man depends on the goals of therapy. We review the most recent developments concerning physiol. **androgen** replacement and inducing virilization, including i.m. **testosterone ester** and the recently approved scrotal transdermal testosterone system. We also review oral androgens and novel **androgen** replacement therapies such as testosterone implants. Restoration of fertility is

possible in the man with secondary hypogonadism. We discuss and compare gonadotropin and gonadotropin-releasing hormone therapy, the two medical therapies for infertility in hypogonadal men.

L8 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:616268 HCAPLUS
DOCUMENT NUMBER: 123:25868
TITLE: Tolerability of intramuscular injections of **testosterone ester** in oil vehicle
AUTHOR(S): Mackey, Mary-Anne; Conway, Ann J.; Handelsman, David J.
CORPORATE SOURCE: Andrology Unit, Royal Prince Alfred Hospital, Sydney, 2006, Australia
SOURCE: Human Reproduction (1995), 10(4), 862-5
CODEN: HUREEE; ISSN: 0268-1161
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors undertook a prospective survey of the tolerability of deep i.m. injections of testosterone enanthate in a castor oil vehicle, the most widely used form of **androgen** replacement therapy. Over a period of 8 mo, 26 men received 551 weekly injections into the gluteal, deltoid or thigh muscle and side-effects were recorded immediately and 1 wk after each injection by the same nurse using a standardized questionnaire. Most injections caused no complaints [389/551, 70.6% (95% confidence interval 66.6-74.4%)] but minor local side-effects, mostly pain and bleeding, were common [162/551, 29.4% (25.6-33.4%)]; no serious side-effects were observed Considering all side-effects, the gluteal site had fewer complaints and was less prone to bleeding but was painful more often than deltoid or thigh injection sites. The laterality of injection at any site had no significant effect on side-effects. The only systemic side effect was episodes of sudden-onset, non-productive cough associated with faintness following eight injections [1.5% (0.6-2.9%)] which the authors speculate may have been due to pulmonary oil microembolism. The authors conclude that, when administered by an experienced nurse, deep i.m. injection of testosterone enanthate in a castor oil vehicle is generally safe and well tolerated but causes relatively frequent minor side-effects, including pain and bleeding. An improved depot form of testosterone would be highly desirable for **androgen** replacement therapy and hormonal male contraception.

L8 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:411783 HCAPLUS
DOCUMENT NUMBER: 122:178690
TITLE: Long-lived testosterone esters in the rat
AUTHOR(S): Borg, Walter; Shackleton, Cedric H. L.; Pahuja, Sham L.; Hochberg, Richard B.
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06510, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1995), 92(5), 1545-9
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Over the past decade it has become increasingly clear that steroid hormones are enzymically esterified with fatty acids. These steroidal esters are the natural analogs of synthetic esters that are used therapeutically. One such family of pharmacol. steroids is the synthetic alkyl esters of testosterone, androgens with great hormonal potency. The

authors have investigated whether testosterone esters exist naturally by using the rat as a model. Most tissues of male rats, including blood, have very little if any ester (quantified by immunoassay as a nonpolar saponifiable metabolite), but fat and testes have sizable quantities, ≈3 ng of testosterone equivalent per g of tissue. Testosterone in fat avs. 9 ng/g. The fat from female rats and long-term (>2 wk) castrated males has no detectable **testosterone ester.** The presence of testosterone esters was confirmed by GC/MS, which clearly showed the presence of testosterone in the hydrolyzed ester fraction of fat from intact males but not long-term castrates. Upon castration, testosterone levels in the fat completely disappear within 6 h. To the contrary, it is not until 48 h after castration that a measurable fall in the **testosterone ester** fraction was observed; even after 10 days a small amount of ester is still present in the fat. These expts. demonstrate the existence of a previously unknown **androgen** with a potentially important physiol. impact; testosterone esters, natural analogs of potent therapeutic agents, occur in the fat where they can serve as a reservoir of preformed **androgen** to stimulate neighboring target tissues.

L8 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:316113 HCAPLUS
DOCUMENT NUMBER: 120:316113
TITLE: Response of adnexal glands to short treatment with high doses of testosterone undecanoate/mesterolone in adult men
AUTHOR(S): Sisci, D.; Aquila, S.; Carpino, A.; Sessa, M.T.; Beraldi, E.; Buffone, M.; Ando, S.
CORPORATE SOURCE: Dep. Cell. Biol., Univ. Calabria, Italy
SOURCE: Advances in Contraceptive Delivery Systems (1993), 9(4), 239-47
CODEN: ACDSEL; ISSN: 1012-8689
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The response of seminal vesicles/prostate to **testosterone ester** administration, as revealed by previous authors, has been attributed partially to a different local conversion of blood testosterone into dihydrotestosterone (DHT). The aim of this study is to compare the effects of testosterone undecanoate administration (200 mg/day for 2 wk) on the adnexal gland response with those of mesterolone (200 mg/day for 2 wk), the 1-α-Me compound of 5-α-DHT which is considered the proper active **androgen** in many **androgen**-dependent target organs. Seminal Zn, prostate acid phosphatase (PAP), prostate-specific antigen (PSA) and fructose were lower on the 14th day of testosterone undecanoate administration with respect to the pretreatment values (B) when free testosterone (AFTC) and free DHT (AFDHTC) circulating levels are maximal, with redns. in PSA and fructose after suspension of the hormone treatment. On the contrary, all biochem. markers tended to be augmented during mesterolone administration and continued, 2 wk after withdrawal of treatment, to be further enhanced, resulting in an increase in prostatic markers. Apparently, prolonged **androgen** exposure in normal man could determine an alteration of sex accessory gland responsiveness as supported by previous exptl. data. To explain the discrepancy between testosterone undecanoate and mesterolone effects on adnexal glands function, it is suggested that the latter treatment in inducing a great enhancement of DHT circulating levels, may elicit a major activation of **androgen** receptor available in adnexal glands and subsequently influence their functional response pattern.

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